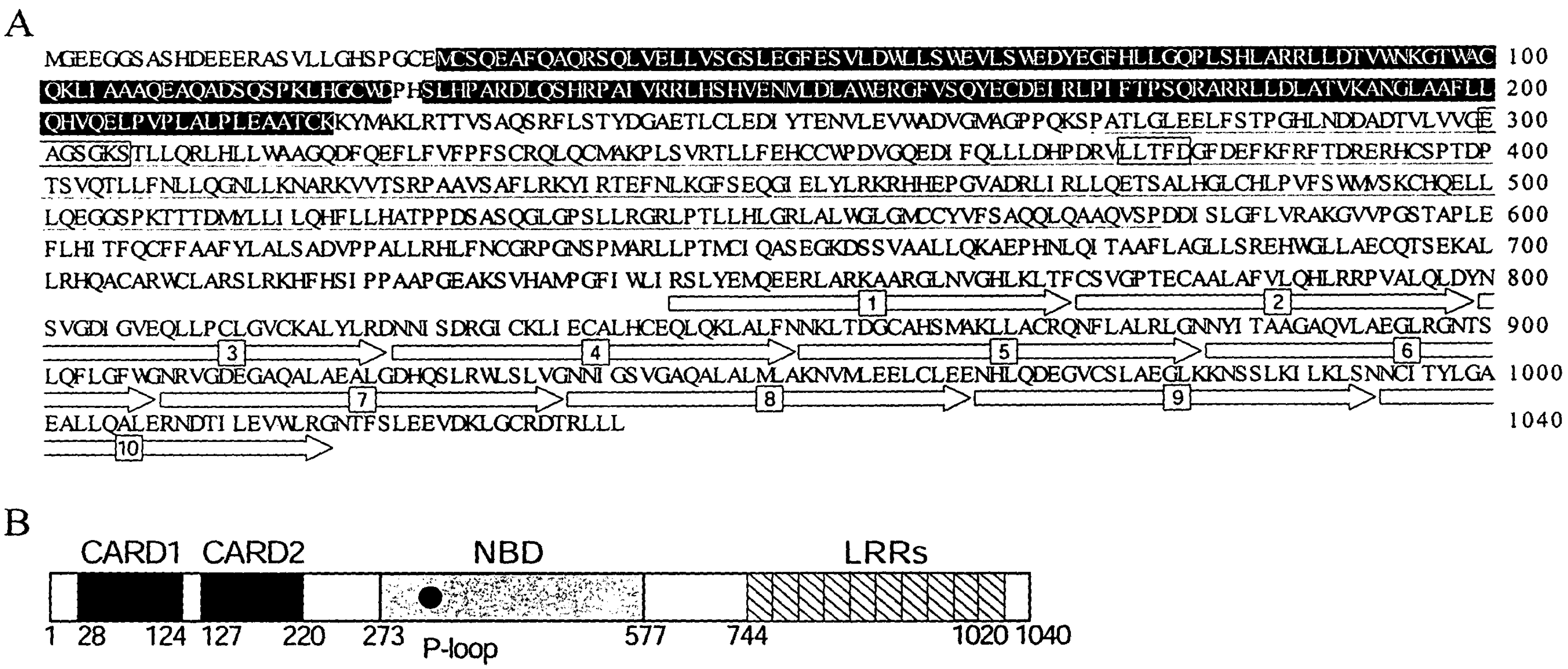

A
MGEEGGSASHDEEERASVLLGHSPGCEMCSQEAFQAQRSQLVELLVSGSLEGFESVLDWLLSWEVLSWEDYEGFHLLGQPLSHLARRLLDTVWNKGTWAC 100
QKLIAAAQEAQADSQSPKLHGCWDPHSLHPARDLQSHRPAIVRRLHSHVENMLDLAWERGFVSQYECDEIRLPIFTPSQRARRLLDLATVKANGLAAFLL 200
QHVQELPVPLALPLEAATCKKYMAKLRTTVSAQSRFLSTYDGAETLCLEDIYTENVLEVVWADVGMAGPPQKSPATLGLEELFSTPGHLNDDADTVLVVGE 300
AGSGKSTLLQRLHLLWAAGQDFQEFLFVFPFSCRQLQCMAKPLSVRTLLFEHCCWPDVGQQEDIFQLLLDHPDRVLLTFDGFDEFKFRFTDRERHCSPTDP 400
TSVQTLLFNLLQGNLLKNARKVVTSRPAAVSAFLRKYIRTEFNLKGFSEQGIELYLRKRHHEPGVADRLIRLLQETSALHGLCHLPVFSWMVSKCHQELL 500
LQEGGSPKTTTDMYLLILQHFLLHATPPDSASQGLGPSLLRGRLPTLLHLGRLALWGLGMCCYVFSAQQLQAAQVSPDDISLGFLVRAKGVVPGSTAPLE 600
FLHITFQCFFAAFYLALSADVPPALLRHLFNCGRPGNSPMARLLPTMCIQASEGKDSSVAALLQKAEPHNLQITAAFLAGLLSREHWGLLAECQTSEKAL 700
LRHQACARWCLARSLRKHFHSIPPAAPGEAKSVHAMPGFIWLIRSLYEMQEERLARKAARGLNVGHLKLTFCSVGPTECAALAFVLQHLRRPVALQLDYN 800
1
2
SVGDIGVEQLLPCLGVCKALYLRDNNISDRGICKLIECALHCEQLQKLALFNNKLTDGCAHSMAKLLACRQNFLALRLGNNYITAAGAQVLAEGLRGNTS 900
3
4
5
6
LQFLGFWGNRVGDEGAQALAEALGDHQSLRWLSLVGNNIGSVGAQALALMLAKNVMLEELCLEENHLQDEGVCSLAEGLKKNSSLKILKLSNNCITYLGA 1000
7
8
9
EALLQALERNDTILEVWLRGNTFSLEEVDKLGCRDTRLLL 1040
10
B
CARD1
CARD2
NBD
LRRs
1
28
124
127
220
273
P-loop
577
744
1020
1040

Figure 1

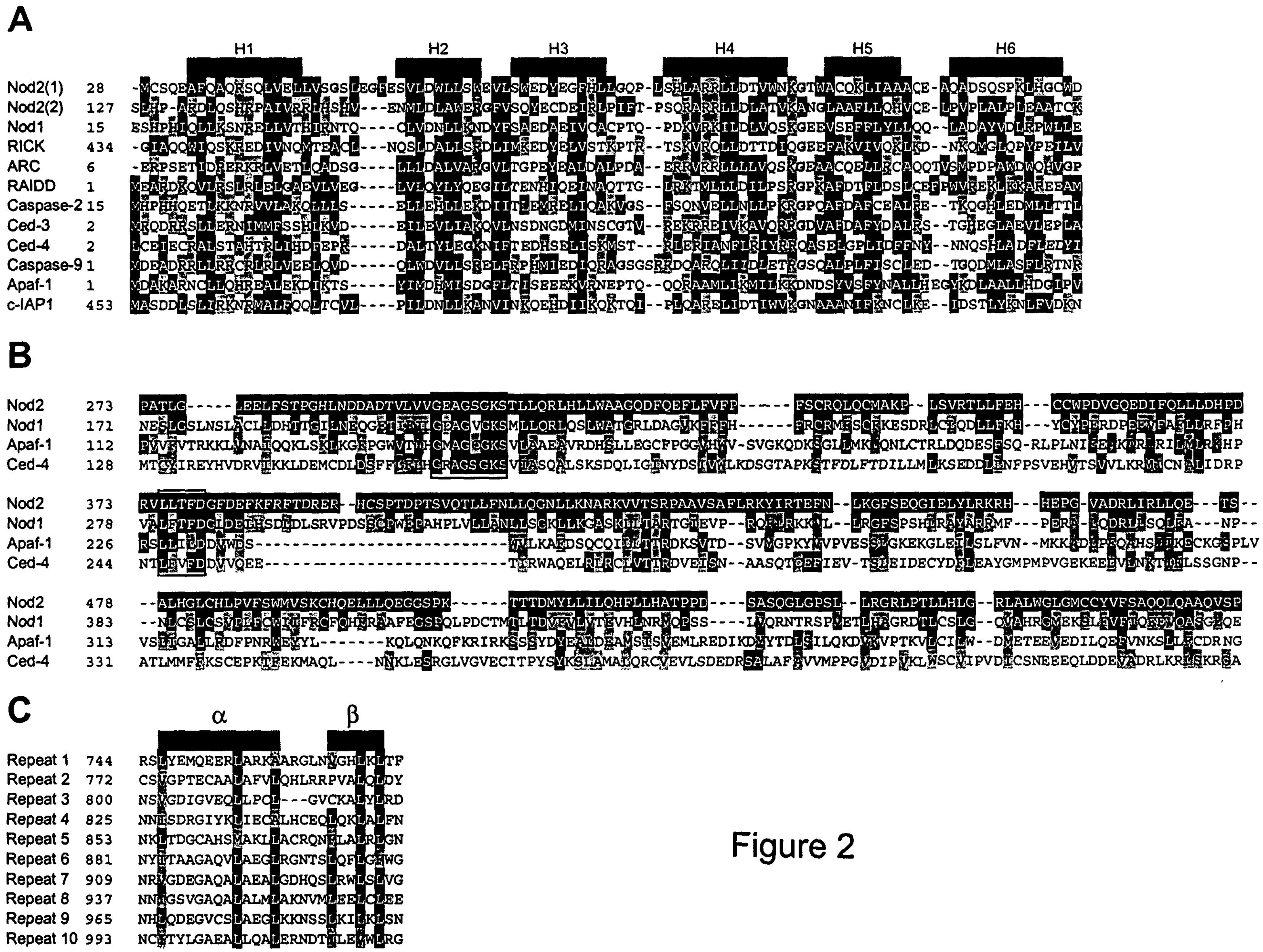
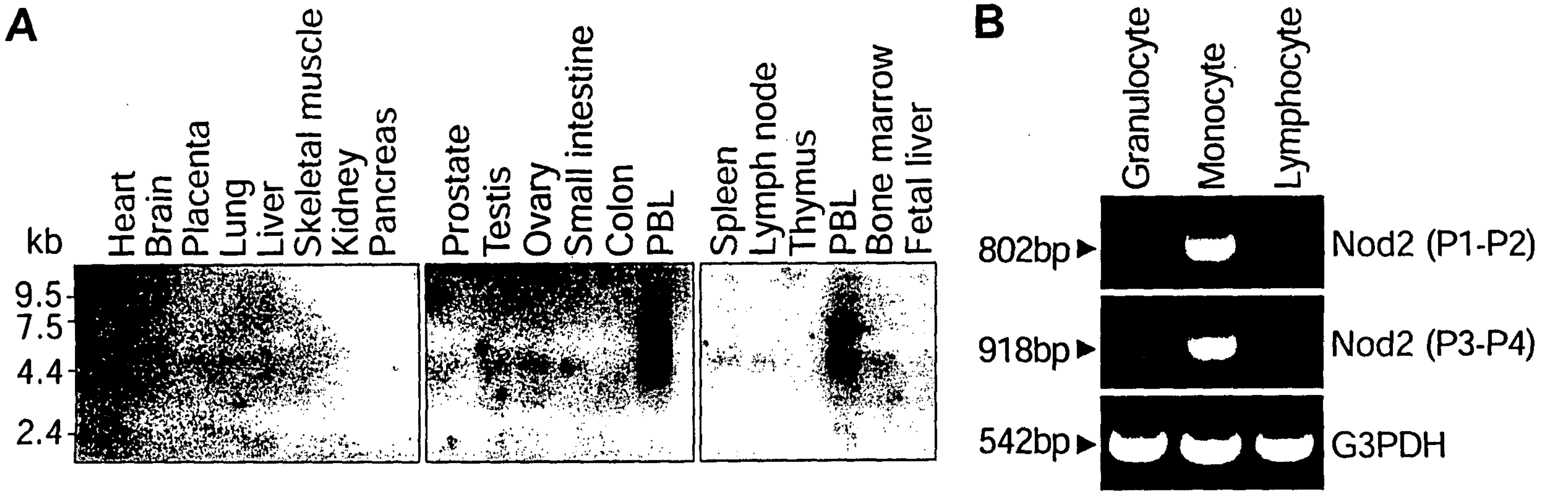

A
H1
H2
H3
H4
H5
H6
Nod2(1) 28
Nod2(2) 127
Nod1 15
RICK 434
ARC 6
RAIDD 1
Caspase-2 15
Ced-3 2
Ced-4 2
Caspase-9 1
Apaf-1 1
c-IAP1 453
B
Nod2 273
Nod1 171
Apaf-1 112
Ced-4 128
Nod2 373
Nod1 278
Apaf-1 226
Ced-4 244
Nod2 478
Nod1 383
Apaf-1 313
Ced-4 331
C
α
β
Repeat 1 744
Repeat 2 772
Repeat 3 800
Repeat 4 825
Repeat 5 853
Repeat 6 881
Repeat 7 909
Repeat 8 937
Repeat 9 965
Repeat 10 993

Figure 2



C

```
GTAGACAGATCCAGGCTCACCAGTCCTGTGCCACTGGGCTTTTGG  45

CGTTCTGCACGAGGCCTACCCGCAGATGCCATGCCTGCTCCCCCA  90

              →
GCCTAATGGCTTTGATGGGGGAAGAGGGTGGTTCAGCCTCTCAC 135
              M  G  E  E  G  G  S  A  S  H

GATGAGGAGGAAAGAGCAAGTGTCCTCCTCGGACATTCTCCGGGT 180
D  E  E  E  R  A  S  V  L  L  G  H  S  P  G
      →
TGTGAAATGTGCTCGCAGGAGGCTTTTCAGGCACAGAGGAGCCAG 225
C  E  M  C  S  Q  E  A  F  Q  A  Q  R  S  Q
```

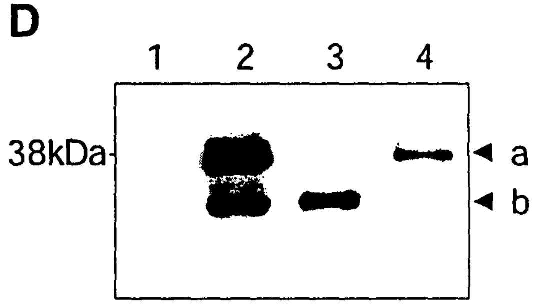


Figure 3

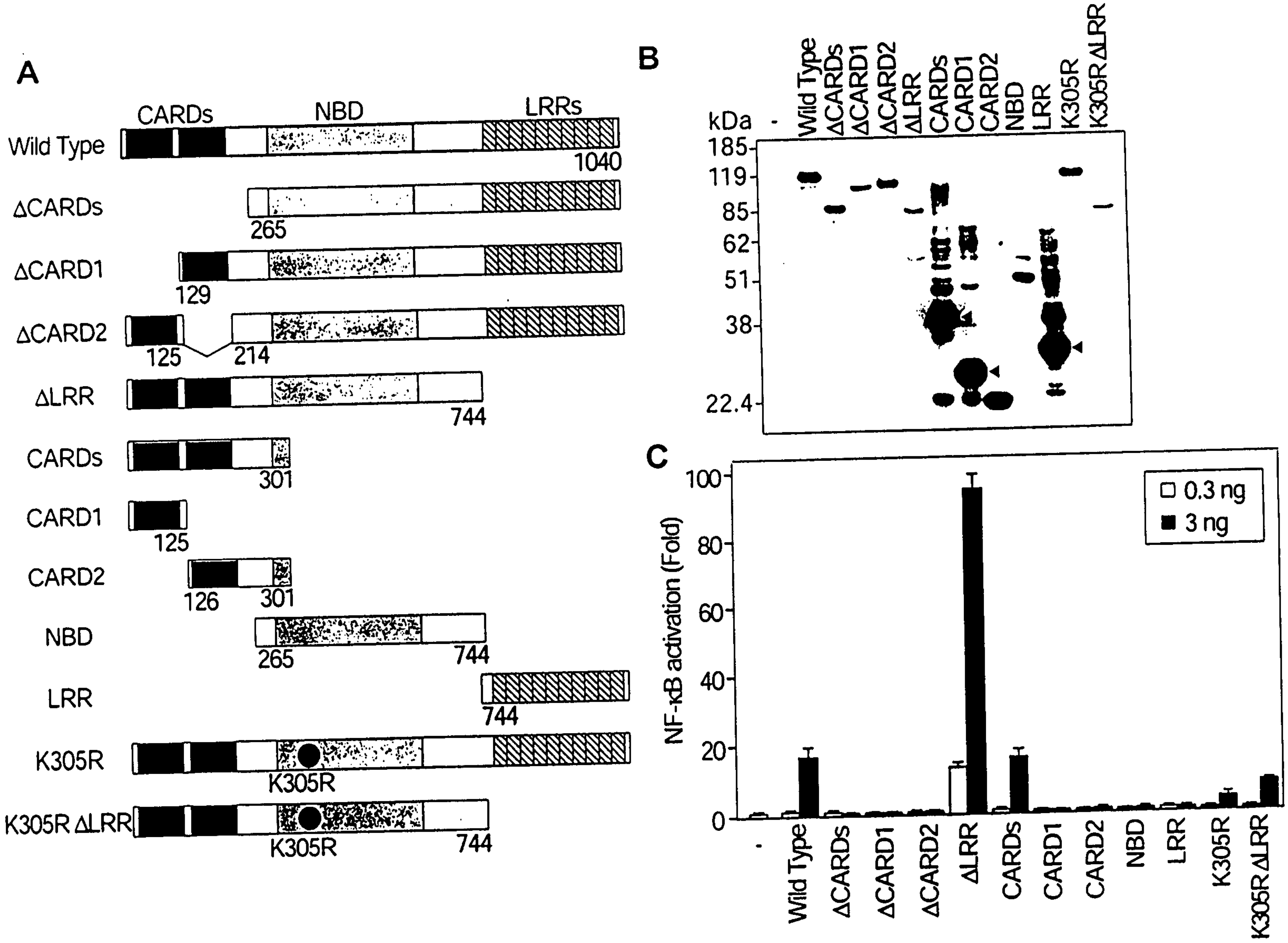

A
CARDs
NBD
LRRs
Wild Type
1040
ΔCARDs
265
ΔCARD1
129
ΔCARD2
125
214
ΔLRR
744
CARDs
301
CARD1
125
CARD2
126
301
NBD
265
744
LRR
744
K305R
K305R
K305R ΔLRR
K305R
744
B
kDa
185
119
85
62
51
38
22.4
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
ΔLRR
CARDs
CARD1
CARD2
NBD
LRR
K305R
K305R ΔLRR
C
NF-κB activation (Fold)
100
80
60
40
20
0
□ 0.3 ng
■ 3 ng
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
ΔLRR
CARDs
CARD1
CARD2
NBD
LRR
K305R
K305R ΔLRR

Figure 4

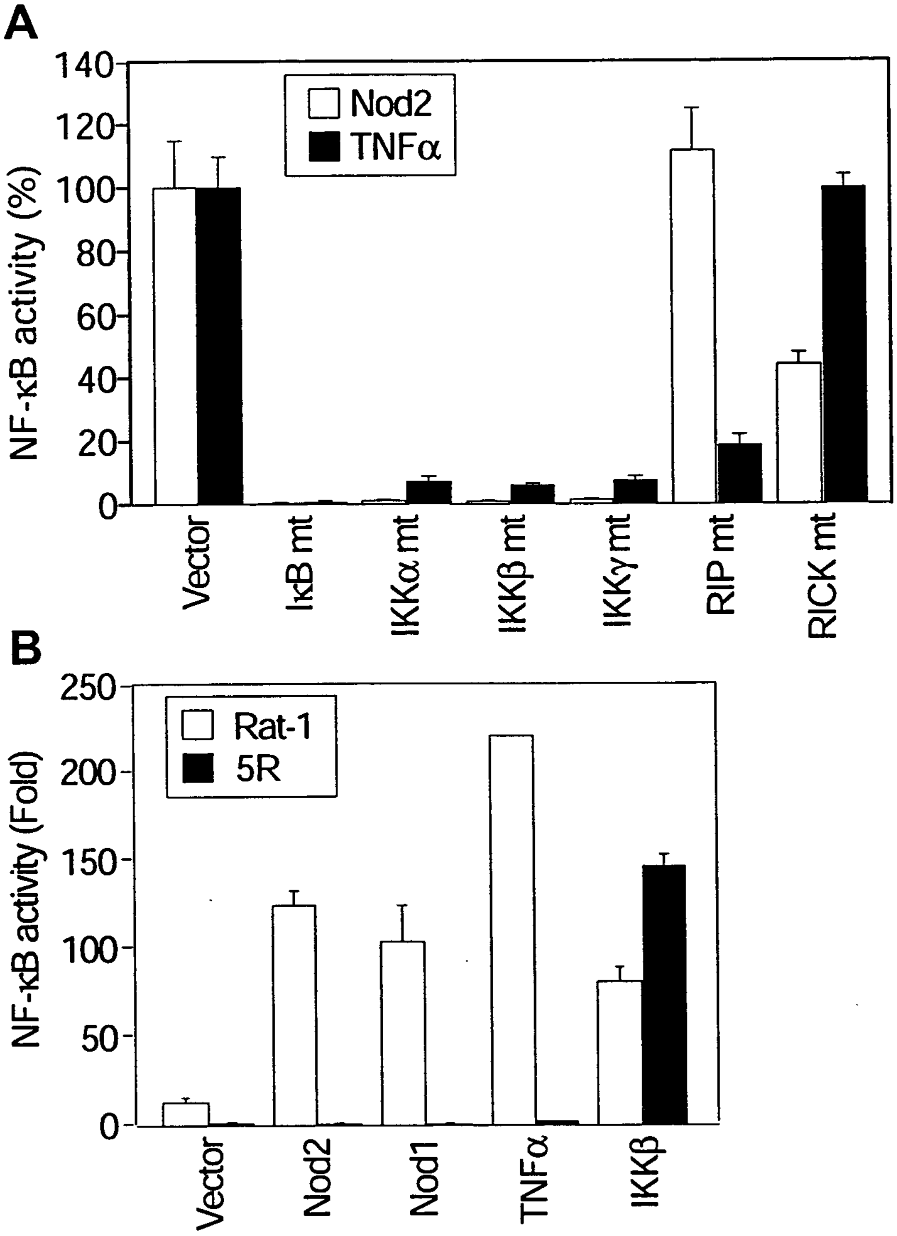

A
NF-κB activity (%)
0
20
40
60
80
100
120
140
Nod2
TNFα
Vector
IκB mt
IKKα mt
IKKβ mt
IKKγ mt
RIP mt
RICK mt
B
NF-κB activity (Fold)
0
50
100
150
200
250
Rat-1
5R
Vector
Nod2
Nod1
TNFα
IKKβ

Figure 5

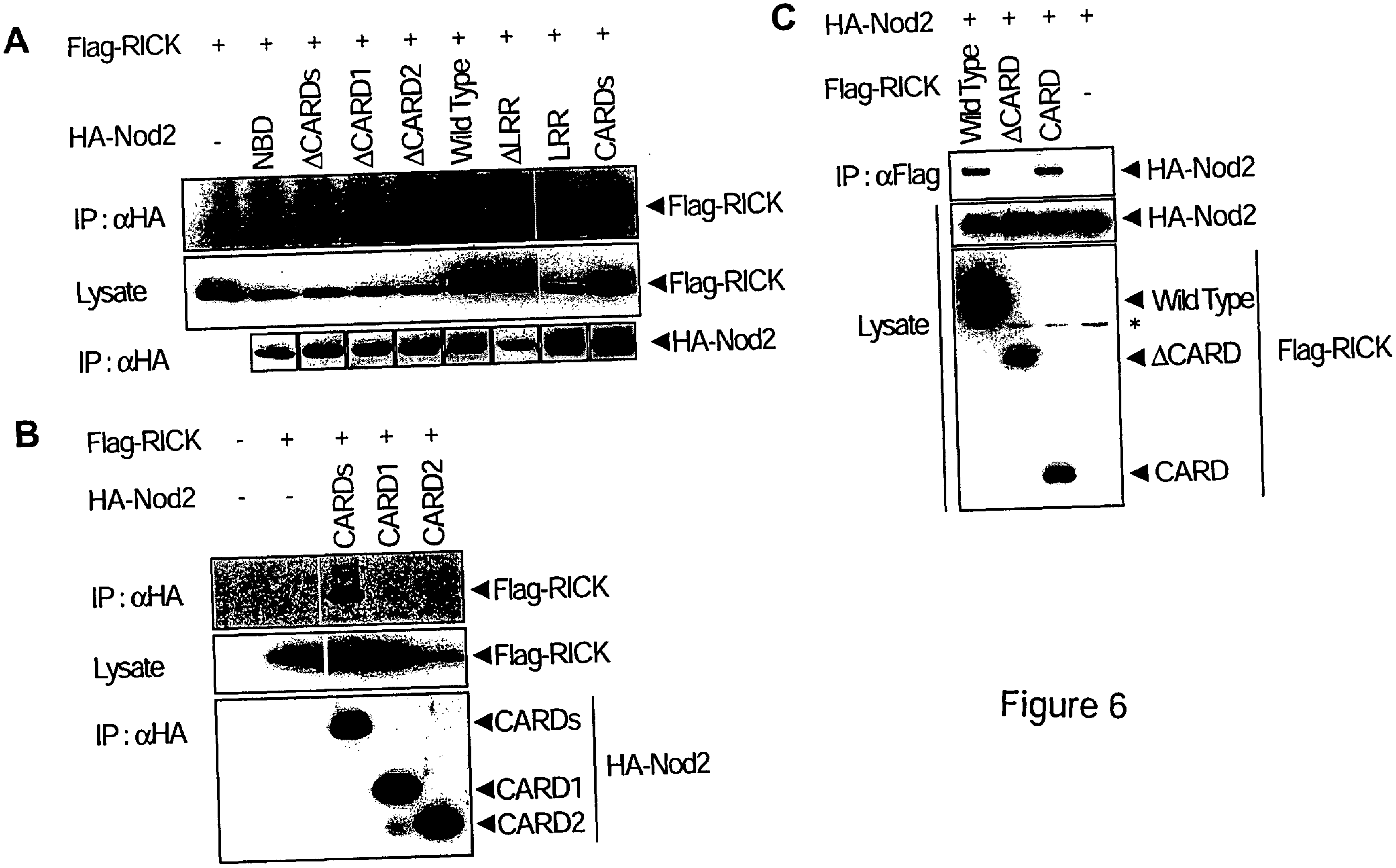

A
Flag-RICK + + + + + + + + +
HA-Nod2 - NBD ΔCARDs ΔCARD1 ΔCARD2 Wild Type ΔLRR LRR CARDs
IP : αHA
◀Flag-RICK
Lysate
◀Flag-RICK
IP : αHA
◀HA-Nod2
B
Flag-RICK - + + + +
HA-Nod2 - - CARDs CARD1 CARD2
IP : αHA
◀Flag-RICK
Lysate
◀Flag-RICK
IP : αHA
◀CARDs
◀CARD1
◀CARD2
HA-Nod2
C
HA-Nod2 + + + +
Flag-RICK Wild Type ΔCARD CARD -
IP : αFlag
◀HA-Nod2
◀HA-Nod2
Lysate
◀Wild Type
*
◀ΔCARD
◀CARD
Flag-RICK

Figure 6

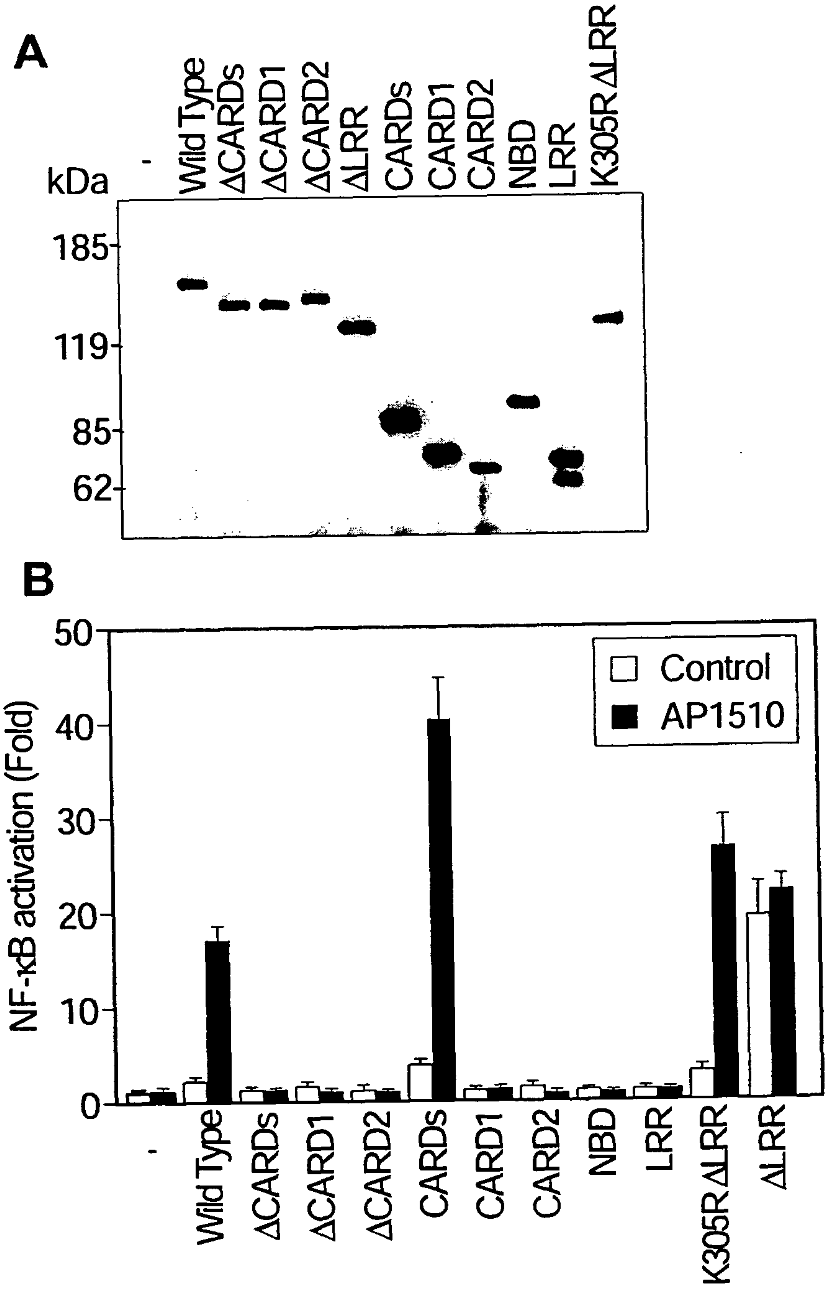

A
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
ΔLRR
CARDs
CARD1
CARD2
NBD
LRR
K305RΔLRR
kDa
185
119
85
62
B
50
40
30
20
10
0
NF-κB activation (Fold)
☐ Control
■ AP1510
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
CARDs
CARD1
CARD2
NBD
LRR
K305RΔLRR
ΔLRR

Figure 7

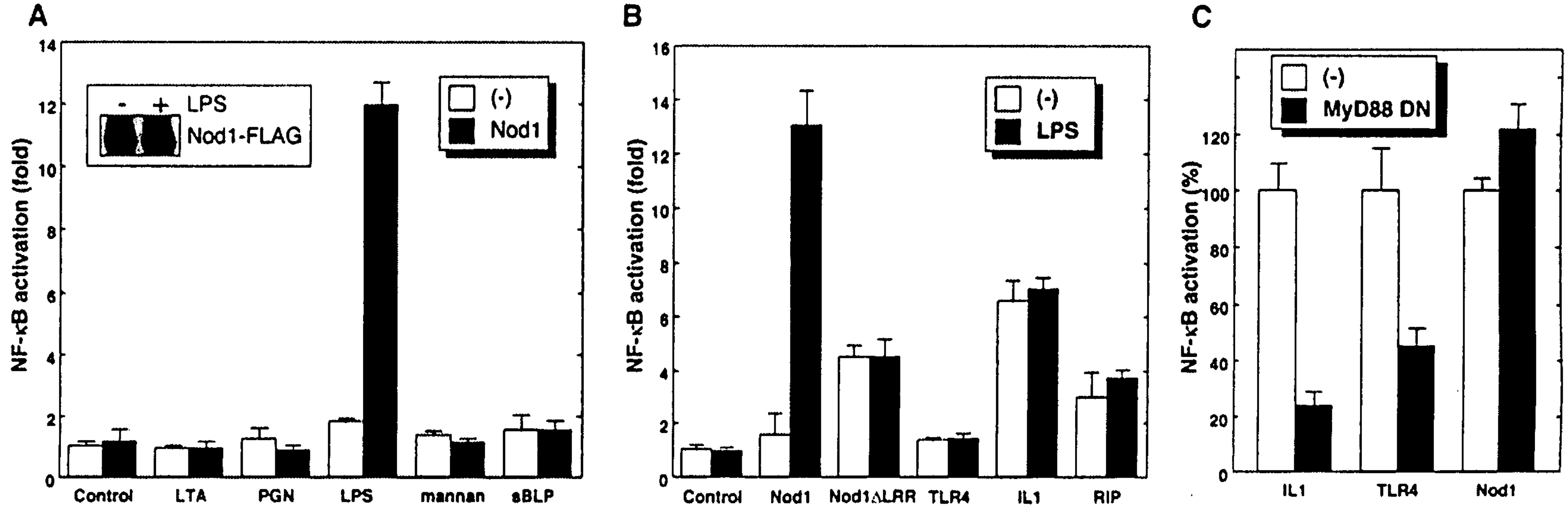

A
NF-κB activation (fold)
0
2
4
6
8
10
12
14
- + LPS
Nod1-FLAG
(-)
Nod1
Control
LTA
PGN
LPS
mannan
sBLP
B
NF-κB activation (fold)
0
2
4
6
8
10
12
14
16
(-)
LPS
Control
Nod1
Nod1ΔLRR
TLR4
IL1
RIP
C
NF-κB activation (%)
0
20
40
60
80
100
120
(-)
MyD88 DN
IL1
TLR4
Nod1

Figure 8

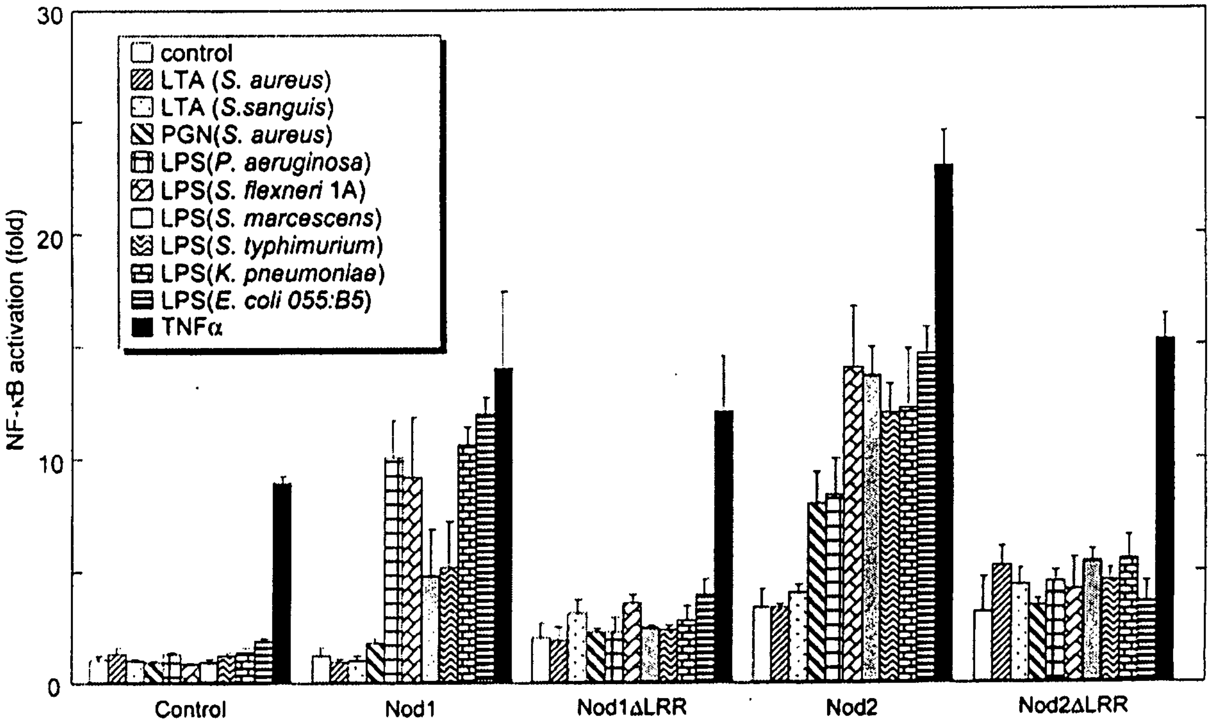

30
20
10
0
NF-κB activation (fold)
☐ control
▨ LTA (*S. aureus*)
☐ LTA (*S.sanguis*)
▧ PGN(*S. aureus*)
⊞ LPS(*P. aeruginosa*)
☒ LPS(*S. flexneri* 1A)
☐ LPS(*S. marcescens*)
▩ LPS(*S. typhimurium*)
⊞ LPS(*K. pneumoniae*)
▤ LPS(*E. coli 055:B5*)
■ TNFα
Control
Nod1
Nod1ΔLRR
Nod2
Nod2ΔLRR

Figure 9

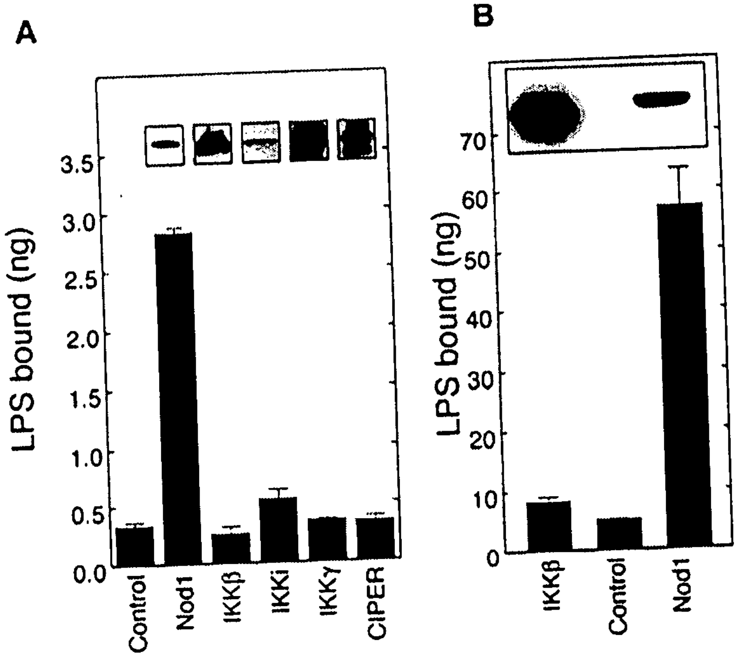

A
LPS bound (ng)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Control
Nod1
IKKβ
IKKi
IKKγ
CIPER
B
LPS bound (ng)
0
10
20
30
40
50
60
70
IKKβ
Control
Nod1

Figure 10

Figure 11

SEQ ID NO:33

Nod2 cDNA sequence

```
gtagacagat ccaggctcac cagtcctgtg ccactgggct tttggcgttc tgcacaaggc      60
ctacccgcag atgccatgcc tgctccccca gcctaatggg ctttgatggg ggaagagggt     120
ggttcagcct ctcacgatga ggaggaaaga gcaagtgtcc tcctcggaca ttctccgggt     180
tgtgaaatgt gctcgcagga ggcttttcag gcacagagga gccagctggt cgagctgctg     240
gtctcagggt ccctggaagg cttcgagagt gtcctggact ggctgctgtc ctgggaggtc     300
ctctcctggg aggactacga gggcttccac ctcctgggcc agcctctctc ccacttggcc     360
aggcgccttc tggacaccgt ctggaataag ggtacttggg cctgtcagaa gctcatcgcg     420
gctgcccaag aagcccaggc cgacagccag tcccccaagc tgcatggctg ctgggacccc     480
cactcgctcc acccagcccg agacctgcag agtcaccggc cagccattgt caggaggctc     540
cacagccatg tggagaacat gctggacctg gcatgggagc ggggtttcgt cagccagtat     600
gaatgtgatg aaatcaggtt gccgatcttc acaccgtccc agagggcaag aaggctgctt     660
gatcttgcca cggtgaaagc gaatggattg gctgccttcc ttctacaaca tgttcaggaa     720
ttaccagtcc cattggccct gcctttggaa gctgccacat gcaagaagta tatggccaag     780
ctgaggacca cggtgtctgc tcagtctcgc ttcctcagta cctatgatgg agcagagacg     840
ctctgcctgg aggacatata cacagagaat gtcctggagg tctgggcaga tgtgggcatg     900
gctggacccc cgcagaagag cccagccacc ctgggcctgg aggagctctt cagcacccct     960
ggccacctca atgacgatgc ggacactgtg ctggtggtgg gtgaggcggg cagtggcaag    1020
agcacgctcc tgcagcggct gcacttgctg tgggctgcag ggcaagactt ccaggaattt    1080
ctctttgtct tcccattcag ctgccggcag ctgcagtgca tggccaaacc actctctgtg    1140
cggactctac tctttgagca ctgctgttgg cctgatgttg gtcaagaaga catcttccag    1200
ttactccttg accaccctga ccgtgtcctg ttaacctttg atggctttga cgagttcaag    1260
ttcaggttca cggatcgtga acgccactgc tccccgaccg accccacctc tgtccagacc    1320
```

ctgctcttca accttctgca gggcaacctg ctgaagaatg cccgcaaggt ggtgaccagc 1380

cgtccggccg ctgtgtcggc gttcctcagg aagtacatcc gcaccgagtt caacctcaag 1440

ggcttctctg aacagggcat cgagctgtac ctgaggaagc gccatcatga gcccggggtg 1500

gcggaccgcc tcatccgcct gctccaagag acctcagccc tgcacggttt gtgccacctg 1560

cctgtcttct catggatggt gtccaaatgc caccaggaac tgttgctgca ggaggggggg 1620

tccccaaaga ccactacaga tatgtacctg ctgattctgc agcattttct gctgcatgcc 1680

acccccccag actcagcttc ccaaggtctg ggacccagtc ttcttcgggg ccgcctcccc 1740

accctcctgc acctgggcag actggctctg tggggcctgg gcatgtgctg ctacgtgttc 1800

tcagcccagc agctccaggc agcacaggtc agccctgatg acatttctct tggcttcctg 1860

gtgcgtgcca aaggtgtcgt gccagggagt acggcgcccc tggaattcct tcacatcact 1920

ttccagtgct tctttgccgc gttctacctg gcactcagtg ctgatgtgcc accagctttg 1980

ctcagacacc tcttcaattg tggcaggcca ggcaactcac caatggccag gctcctgccc 2040

acgatgtgca tccaggcctc ggagggaaag gacagcagcg tggcagcttt gctgcagaag 2100

gccgagccgc acaaccttca gatcacagca gccttcctgg cagggctgtt gtcccgggag 2160

cactggggcc tgctggctga gtgccagaca tctgagaagg ccctgctccg gcgccaggcc 2220

tgtgcccgct ggtgtctggc ccgcagcctc cgcaagcact tccactccat cccgccagct 2280

gcaccgggtg aggccaagag cgtgcatgcc atgcccgggt tcatctggct catccggagc 2340

ctgtacgaga tgcaggagga gcggctggct cggaaggctg cacgtggcct gaatgttggg 2400

cacctcaagt tgacattttg cagtgtgggc cccactgagt gtgctgccct ggcctttgtg 2460

ctgcagcacc tccggcggcc cgtggccctg cagctggact acaactctgt gggtgacatt 2520

ggcgtggagc agctgctgcc ttgccttggt gtctgcaagg ctctgtattt gcgcgataac 2580

aatatctcag accgaggcat ctgcaagctc attgaatgtg ctcttcactg cgagcaattg 2640

cagaagttag ctctattcaa caacaaattg actgacggct gtgcacactc catggctaag 2700

ctccttgcat gcaggcagaa cttcttggca ttgaggctgg ggaataacta catcactgcc 2760

gcgggagccc aagtgctggc cgaggggctc cgaggcaaca cctccttgca gttcctggga 2820

ttctggggca acagagtggg tgacgagggg gcccaggccc tggctgaagc cttgggtgat 2880

caccagagct tgaggtggct cagcctggtg gggaacaaca ttggcagtgt gggtgcccaa 2940

gccttggcac tgatgctggc aaagaacgtc atgctagaag aactctgcct ggaggagaac 3000

catctccagg atgaaggtgt atgttctctc gcagaaggac tgaagaaaaa ttcaagtttg 3060

aaaatcctga agttgtccaa taactgcatc acctacctag ggcagaagcc cctcctgcag 3120

```
gccccttgaaa ggaatgacac catcctggaa gtctggctcc gagggaacac tttctctcta      3180
gaggaggttg acaagctcgg ctgcagggac accagactct tgctttgaag tctccgggag      3240
gatgttcgtc tcagtttgtt tgtgagcagg ctgtgagttt gggccccaga ggctgggtga      3300
catgtgttgg cagcctcttc aaaatgagcc ctgtcctgcc taaggctgaa cttgttttct      3360
gggaacacca taggtcacct ttattctggc agaggaggga gcatcagtgc cctccaggat      3420
agacttttcc caagcctact tttgccattg acttcttccc aagattcaat cccaggatgt      3480
acaaggacag cccctcctcc atagtatggg actggcctct gctgatcctc ccaggcttcc      3540
gtgtgggtca gtggggccca tggatgtgct tgttaactga gtgccttttg gtggagaggc      3600
ccggcctctc acaaaagacc ccttaccact gctctgatga agaggagtac acagaacaca      3660
taattcagga agcagctttc cccatgtctc gactcatcca tccaggccat tccccgtctc      3720
tggttcctcc cctcctcctg gactcctgca cacgctcctt cctctgaggc tgaaattcag      3780
aatattagtg acctcagctt tgatatttca cttacagcac ccccaaccct ggcacccagg      3840
gtgggaaggg ctacacctta gcctgccctc ctttccggtg tttaagacat ttttggaagg      3900
ggacacgtga cagccgtttg ttccccaaga cattctaggt ttgcaagaaa aatatgacca      3960
cactccagct gggatcacat gtggactttt atttccagtg aaatcagtta ctcttcagtt      4020
aagcctttgg aaacagctcg actttaaaaa gctccaaatg cagctttaaa aaattaatct      4080
gggccagaat ttcaaacggc ctcactaggc ttctggttga tgcctgtgaa ctgaactctg      4140
acaacagact tctgaaatag acccacaaga ggcagttcca tttcatttgt gccagaatgc      4200
tttaggatgt acagttatgg attgaaagtt tacaggaaaa aaaattaggc cgttccttca      4260
aagcaaatgt cttcctggat tattcaaaat gatgtatgtt gaagcctttg taaattgtca      4320
gatgctgtgc aaatgttatt attttaaaca ttatgatgtg tgaaaactgg ttaatattta      4380
taggtcactt tgttttactg tcttaagttt atactcttat agacaacatg gccgtgaact      4440
ttatgctgta aataatcaga ggggaataaa ctgttgagtc aaaac                     4485
```

Figure 12

SEQ ID NO:1

Nod2 cDNA sequence

```
gtagacagat ccaggctcac cagtcctgtg ccactgggct tttggcgttc tgcacaaggc      60
ctacccgcag atgccatgcc tgctccccca gcctaatggg ctttgatggg ggaagagggt     120
ggttcagcct ctcacgatga ggaggaaaga gcaagtgtcc tcctcggaca ttctccgggt     180
tgtgaaatgt gctcgcagga ggcttttcag gcacagagga gccagctggt cgagctgctg     240
gtctcagggt ccctggaagg cttcgagagt gtcctggact ggctgctgtc ctgggaggtc     300
ctctcctggg aggactacga gggcttccac ctcctgggcc agcctctctc ccacttggcc     360
aggcgccttc tggacaccgt ctggaataag ggtacttggg cctgtcagaa gctcatcgcg     420
gctgcccaag aagcccaggc cgacagccag tcccccaagc tgcatggctg ctgggacccc     480
cactcgctcc acccagcccg agacctgcag agtcaccggc cagccattgt caggaggctc     540
cacagccatg tggagaacat gctggacctg gcatgggagc ggggtttcgt cagccagtat     600
gaatgtgatg aaatcaggtt gccgatcttc acaccgtccc agagggcaag aaggctgctt     660
gatcttgcca cggtgaaagc gaatggattg gctgccttcc ttctacaaca tgttcaggaa     720
ttaccagtcc cattggccct gcctttggaa gctgccacat gcaagaagta tatggccaag     780
ctgaggacca cggtgtctgc tcagtctcgc ttcctcagta cctatgatgg agcagagacg     840
ctctgcctgg aggacatata cacagagaat gtcctggagg tctgggcaga tgtgggcatg     900
gctggacccc cgcagaagag cccagccacc ctgggcctgg aggagctctt cagcacccct     960
ggccacctca atgacgatgc ggacactgtg ctggtggtgg gtgaggcggg cagtggcaag    1020
agcacgctcc tgcagcggct gcacttgctg tgggctgcag ggcaagactt ccaggaattt    1080
ctctttgtct tcccattcag ctgccggcag ctgcagtgca tggccaaacc actctctgtg    1140
cggactctac tctttgagca ctgctgttgg cctgatgttg gtcaagaaga catcttccag    1200
ttactccttg accaccctga ccgtgtcctg ttaacctttg atggctttga cgagttcaag    1260
ttcaggttca cggatcgtga acgccactgc tccccgaccg accccacctc tgtccagacc    1320
```

```
ctgctcttca accttctgca gggcaacctg ctgaagaatg cccgcaaggt ggtgaccagc      1380

cgtccggccg ctgtgtcggc gttcctcagg aagtacatcc gcaccgagtt caacctcaag      1440

ggcttctctg aacagggcat cgagctgtac ctgaggaagc gccatcatga gcccggggtg      1500

gcggaccgcc tcatccgcct gctccaagag acctcagccc tgcacggttt gtgccacctg      1560

cctgtcttct catggatggt gtccaaatgc caccaggaac tgttgctgca ggaggggggg      1620

tccccaaaga ccactacaga tatgtacctg ctgattctgc agcatttcct gctgcatgcc      1680

acccccccag actcagcttc ccaaggtctg ggacccagtc ttcttcgggg ccgcctcccc      1740

accctcctgc acctgggcag actggctctg tggggcctgg gcatgtgctg ctacgtgttc      1800

tcagcccagc agctccaggc agcacaggtc agccctgatg acatttctct tggcttcctg      1860

gtgcgtgcca aaggtgtcgt gccagggagt acggcgcccc tggaattcct tcacatcact      1920

ttccagtgct tctttgccgc gttctacctg gcactcagtg ctgatgtgcc accagctttg      1980

ctcagacacc tcttcaattg tggcaggcca ggcaactcac caatggccag gctcctgccc      2040

acgatgtgca tccaggcctc ggagggaaag gacagcagcg tggcagcttt gctgcagaag      2100

gccgagccgc acaaccttca gatcacagca gccttcctgg cagggctgtt gtcccgggag      2160

cactggggcc tgctggctga gtgccagaca tctgagaagg ccctgctccg gcgccaggcc      2220

tgtgcccgct ggtgtctggc ccgcagcctc cgcaagcact tccactccat cccgccagct      2280

gcaccgggtg aggccaagag cgtgcatgcc atgcccgggt tcatctggct catccggagc      2340

ctgtacgaga tgcaggagga gcggctggct cggaaggctg cacgtggcct gaatgttggg      2400

cacctcaagt tgacattttg cagtgtgggc cccactgagt gtgctgccct ggcctttgtg      2460

ctgcagcacc tccggcggcc cgtggccctg cagctggact acaactctgt gggtgacatt      2520

ggcgtggagc agctgctgcc ttgccttggt gtctgcaagg ctctgtattt gcgcgataac      2580

aatatctcag accgaggcat ctgcaagctc attgaatgtg ctcttcactg cgagcaattg      2640

cagaagttag ctctattcaa caacaaattg actgacggct gtgcacactc catggctaag      2700

ctccttgcat gcaggcagaa cttcttggca ttgaggctgg ggaataacta catcactgcc      2760

gcgggagccc aagtgctggc cgaggggctc cgaggcaaca cctccttgca gttcctggga      2820

ttctggggca acagagtggg tgacgagggg gcccaggccc tggctgaagc cttgggtgat      2880

caccagagct tgaggtggct cagcctggtg gggaacaaca ttggcagtgt gggtgcccaa      2940

gccttggcac tgatgctggc aaagaacgtc atgctagaag aactctgcct ggaggagaac      3000

catctccagg atgaaggtgt atgttctctc gcagaaggac tgaagaaaaa ttcaagtttg      3060

aaaatcctga agttgtccaa taactgcatc acctacctag ggcagaagcc cctcctgcag      3120
```

```
gcccttgaaa ggaatgacac catcctggaa gtctggctcc gagggaacac tttctctcta      3180
gaggaggttg acaagctcgg ctgcagggac accagactct tgctttgaag tctccgggag      3240
gatgttcgtc tcagtttgtt tgtgagcagg ctgtgagttt gggccccaga ggctgggtga      3300
catgtgttgg cagcctcttc aaaatgagcc ctgtcctgcc taaggctgaa cttgttttct      3360
gggaacacca taggtcacct ttattctggc agaggaggga gcatcagtgc cctccaggat      3420
agacttttcc caagcctact tttgccattg acttcttccc aagattcaat cccaggatgt      3480
acaaggacag cccctcctcc atagtatggg actggcctct gctgatcctc ccaggcttcc      3540
gtgtgggtca gtggggccca tggatgtgct tgttaactga gtgccttttg gtggagaggc      3600
ccggcctctc acaaaagacc ccttaccact gctctgatga agaggagtac acagaacaca      3660
taattcagga agcagctttc cccatgtctc gactcatcca tccaggccat tccccgtctc      3720
tggttcctcc cctcctcctg gactcctgca cacgctcctt cctctgaggc tgaaattcag      3780
aatattagtg acctcagctt tgatatttca cttacagcac ccccaaccct ggcacccagg      3840
gtgggaaggg ctacacctta gcctgccctc ctttccggtg tttaagacat ttttggaagg      3900
ggacacgtga cagccgtttg ttccccaaga cattctaggt ttgcaagaaa aatatgacca      3960
cactccagct gggatcacat gtggactttt atttccagtg aaatcagtta ctcttcagtt      4020
aagcctttgg aaacagctcg actttaaaaa gctccaaatg cagctttaaa aaattaatct      4080
gggccagaat ttcaaacggc ctcactaggc ttctggttga tgcctgtgaa ctgaactctg      4140
acaacagact tctgaaatag acccacaaga ggcagttcca tttcatttgt gccagaatgc      4200
tttaggatgt acagttatgg attgaaagtt tacaggaaaa aaaattaggc cgttccttca      4260
aagcaaatgt cttcctggat tattcaaaat gatgtatgtt gaagcctttg taaattgtca      4320
gatgctgtgc aaatgttatt attttaaaca ttatgatgtg tgaaaactgg ttaatattta      4380
taggtcactt tgttttactg tcttaagttt atactcttat agacaacatg gccgtgaact      4440
ttatgctgta aataatcaga ggggaataaa ctgttgagtc aaaac                      4485
```

Figure 13

SEQ ID NO:2

MGEEGGSASH DEEERASVLL GHSPGCEMCS QEAFQAQRSQ LVELLVSGSL EGFESVLDWL
LSWEVLSWED YEGFHLLGQP LSHLARRLLD TVWNKGTWAC QKLIAAAQEA QADSQSPKLH
GCWDPHSLHP ARDLQSHRPA IVRRLHSHVE NMLDLAWERG FVSQYECDEI RLPIFTPSQR
ARRLLDLATV KANGLAAFLL QHVQELPVPL ALPLEAATCK KYMAKLRTTV SAQSRFLSTY
DGAETLCLED IYTENVLEVW ADVGMAGPPQ KSPATLGLEE LFSTPGHLND DADTVLVVGE
AGSGKSTLLQ RLHLLWAAGQ DFQEFLFVFP FSCRQLQCMA KPLSVRTLLF EHCCWPDVGQ
EDIFQLLLDH PDRVLLTFDG FDEFKFRFTD RERHCSPTDP TSVQTLLFNL LQGNLLKNAR
KVVTSRPAAV SAFLRKYIRT EFNLKGFSEQ GIELYLRKRH HEPGVADRLI RLLQETSALH
GLCHLPVFSW MVSKCHQELL LQEGGSPKTT TDMYLLILQH FLLHATPPDS ASQGLGPSLL
RGRLPTLLHL GRLALWGLGM CCYVFSAQQL QAAQVSPDDI SLGFLVRAKG VVPGSTAPLE
FLHITFQCFF AAFYLALSAD VPPALLRHLF NCGRPGNSPM ARLLPTMCIQ ASEGKDSSVA
ALLQKAEPHN LQITAAFLAG LLSREHWGLL AECQTSEKAL LRRQACARWC LARSLRKHFH
SIPPAAPGEA KSVHAMPGFI WLIRSLYEMQ EERLARKAAR GLNVGHLKLT FCSVGPTECA
ALAFVLQHLR RPVALQLDYN SVGDIGVEQL LPCLGVCKAL YLRDNNISDR GICKLIECAL
HCEQLQKLAL FNNKLTDGCA HSMAKLLACR QNFLALRLGN NYITAAGAQV LAEGLRGNTS
LQFLGFWGNR VGDEGAQALA EALGDHQSLR WLSLVGNNIG SVGAQALALM LAKNVMLEEL
CLEENHLQDE GVCSLAEGLK KNSSLKILKL SNNCITYLGA EALLQALERN DTILEVWLRG
NTFSLEEVDK LGCRDTRLLL *

Figure 14

SEQ ID NO:3

MCSQEAFQAQ RSQLVELLVS GSLEGFESVL DWLLSWEVLS WEDYEGFHLL GQPLSHLARR

LLDTVWNKGT WACQKLIAAA QEAQADSQSP KLHGCWDPHS LHPARDLQSH RPAIVRRLHS

HVENMLDLAW ERGFVSQYEC DEIRLPIFTP SQRARRLLDL ATVKANGLAA FLLQHVQELP

VPLALPLEAA TCKKYMAKLR TTVSAQSRFL STYDGAETLC LEDIYTENVL EVWADVGMAG

PPQKSPATLG LEELFSTPGH LNDDADTVLV VGEAGSGKST LLQRLHLLWA AGQDFQEFLF

VFPFSCRQLQ CMAKPLSVRT LLFEHCCWPD VGQEDIFQLL LDHPDRVLLT FDGFDEFKFR

FTDRERHCSP TDPTSVQTLL FNLLQGNLLK NARKVVTSRP AAVSAFLRKY IRTEFNLKGF

SEQGIELYLR KRHHEPGVAD RLIRLLQETS ALHGLCHLPV FSWMVSKCHQ ELLLQEGGSP

KTTTDMYLLI LQHFLLHATP PDSASQGLGP SLLRGRLPTL LHLGRLALWG LGMCCYVFSA

QQLQAAQVSP DDISLGFLVR AKGVVPGSTA PLEFLHITFQ CFFAAFYLAL SADVPPALLR

HLFNCGRPGN SPMARLLPTM CIQASEGKDS SVAALLQKAE PHNLQITAAF LAGLLSREHW

GLLAECQTSE KALLRRQACA RWCLARSLRK HFHSIPPAAP GEAKSVHAMP GFIWLIRSLY

EMQEERLARK AARGLNVGHL KLTFCSVGPT ECAALAFVLQ HLRRPVALQL DYNSVGDIGV

EQLLPCLGVC KALYLRDNNI SDRGICKLIE CALHCEQLQK LALFNNKLTD GCAHSMAKLL

ACRQNFLALR LGNNYITAAG AQVLAEGLRG NTSLQFLGFW GNRVGDEGAQ ALAEALGDHQ

SLRWLSLVGN NIGSVGAQAL ALMLAKNVML EELCLEENHL QDEGVCSLAE GLKKNSSLKI

LKLSNNCITY LGAEALLQAL ERNDTILEVW LRGNTFSLEE VDKLGCRDTR LLL*

Figure 15
SEQ ID NO:34

Nod2a AA sequence, Mutant

MGEEGGSASH DEEERASVLL GHSPGCEMCS QEAFQAQRSQ LVELLVSGSL EGFESVLDWL

LSWEVLSWED YEGFHLLGQP LSHLARRLLD TVWNKGTWAC QKLIAAAQEA QADSQSPKLH

GCWDPHSLHP ARDLQSHRPA IVRRLHSHVE NMLDLAWERG FVSQYECDEI RLPIFTPSQR

ARRLLDLATV KANGLAAFLL QHVQELPVPL ALPLEAATCK KYMAKLRTTV SAQSRFLSTY

DGAETLCLED IYTENVLEVW ADVGMAGPPQ KSPATLGLEE LFSTPGHLND DADTVLVVGE

AGSGKSTLLQ RLHLLWAAGQ DFQEFLFVFP FSCRQLQCMA KPLSVRTLLF EHCCWPDVGQ

EDIFQLLLDH PDRVLLTFDG FDEFKFRFTD RERHCSPTDP TSVQTLLFNL LQGNLLKNAR

KVVTSRPAAV SAFLRKYIRT EFNLKGFSEQ GIELYLRKRH HEPGVADRLI RLLQETSALH

GLCHLPVFSW MVSKCHQELL LQEGGSPKTT TDMYLLILQH FLLHATPPDS ASQGLGPSLL

RGRLPTLLHL GRLALWGLGM CCYVFSAQQL QAAQVSPDDI SLGFLVRAKG VVPGSTAPLE

FLHITFQCFF AAFYLALSAD VPPALLRHLF NCGRPGNSPM ARLLPTMCIQ ASEGKDSSVA

ALLQKAEPHN LQITAAFLAG LLSREHWGLL AECQTSEKAL LRRQACARWC LARSLRKHFH

SIPPAAPGEA KSVHAMPGFI WLIRSLYEMQ EERLARKAAR GLNVGHLKLT FCSVGPTECA

ALAFVLQHLR RPVALQLDYN SVGDIGVEQL LPCLGVCKAL YLRDNNISDR GICKLIECAL

HCEQLQKLAL FNNKLTDGCA HSMAKLLACR QNFLALRLGN NYITAAGAQV LAEGLRGNTS

LQFLGFWGNR VGDEGAQALA EALGDHQSLR WLSLVGNNIG SVGAQALALM LAKNVMLEEL

CLEENHLQDE GVCSLAEGLK KNSSLKILKL SNNCITYLGA EALLQAP*

FIGURE 16

Nod2 Exon11, Wild type

cagacatgag caggatgtgt ctaagggaca ggtgggcttc agtagactgg ctaactcctg

cagtctcttt aactggacag tttcaagagg aaaaccaaga atccttgaag ctcaccattg

tatcttcttt tccagGTTGT CCAATAACTG CATCACCTAC CTAGGGGCAG AAGCCCTCCT
L S N N C I T Y L G A E A L L

GCAGGCCCTT GAAAGGAATG ACACCATCCT GGAAGTCTGg taaggcccct gggcaggcct
Q A L E R N D T I L E V

gttttagctc tccgaacctc agtttttcta tctgtaaaat ggggtgacgg gagagaggaa

tggcagaatt ttgaggatcc cttctgattc tgacattcag tgagaatgat tctgcatgtg

Nod2 Exon11, Mutant

cagacatgag caggatgtgt ctaagggaca ggtgggcttc agtagactgg ctaactcctg

cagtctcttt aactggacag tttcaagagg aaaaccaaga atccttgaag ctcaccattg

tatcttcttt tccagGTTGT CCAATAACTG CATCACCTAC CTAGGGGCAG AAGCCCTCCT
L S N N C I T Y L G A E A L L

GCAGGCCCCT TGAAAGGAAT GACACCATCC TGGAAGTCTG gtaaggcccc tgggcaggcc

Q A P *

tgttttagct ctccgaacct cagtttttct atctgtaaaa tggggtgacg ggagagagga

atggcagaat tttgaggatc ccttctgatt ctgacattca gtgagaatga ttctgcatgt

g